

WHAT IS CLAIMED IS:

- 1 1. An isolated nucleic acid molecule encoding a replication competent recombinant
2 Hepatitis C Virus (HCV) genome, which nucleic acid comprises all or part of an HCV
3 genome and is able to replicate efficiently when transfected into a susceptible cell line
4 without reducing the growth rate of said cell line by more than 10 fold.
- 1 2. The isolated nucleic acid molecule encoding a recombinant HCV genome of claim 1,
2 which nucleic acid comprises from 5' to 3' on the positive-sense nucleic acid
 - 3 (a) a functional 5' HCV non-translated region (NTR) comprising an extreme
4 5'-terminal conserved sequence;
 - 5 (b) at least one open reading frame (ORF) encoding a heterologous gene
6 operatively associated with an expression control sequence, wherein the
7 heterologous gene and expression control sequence are oriented on the
8 positive-strand nucleic acid molecule;
 - 9 (c) an ORF encoding at least a portion of an HCV polyprotein whose cleavage
10 products form functional components of HCV virus particles and RNA
11 replication machinery, and
 - 12 (d) an HCV 3' NTR comprising an extreme 3'-terminal conserved sequence,
13 and wherein said nucleic acid is able to replicate efficiently in a susceptible
14 cell line without reducing the growth rate of said cell line by more than 10
15 fold.
- 1 3. The isolated nucleic acid of claim 1, wherein the susceptible cell line is selected from
2 the group consisting of human hepatoma cell line Huh-7, human hepatoma cell line
3 HepG2, hepatoma cell line PH5CH, *T. belangeri* liver cell line MBTL, human diploid
4 fibroblast cell line VERO, secondary monkey kidney cell line CV-1, T cell line MT-2,
5 T cell line HPBMA10-2, T cell line MOLT-4, and B cell line Daudi.

- 1 4. The susceptible cell line of claim 4, which is human hepatoma cell line Huh-7.
- 1 5. The isolated nucleic acid molecule according to claim 1, which is selected from the
2 group consisting of double stranded DNA, single stranded DNA, double stranded
3 RNA, and single stranded RNA.
- 1 6. An isolated nucleic acid molecule which is not more than 99.9% identical and is at
2 least 95% identical to SEQ ID NO: 1.
- 1 7. The isolated nucleic acid molecule of claim 6 comprising nucleotide sequence of
2 HCVR 2 (SEQ ID NO: 2).
- 1 8. The isolated nucleic acid molecule of claim 6 comprising nucleotide sequence of
2 HCVR 8 (SEQ ID NO: 3).
- 1 9. The isolated nucleic acid molecule of claim 6 comprising nucleotide sequence of
2 HCVR 9 (SEQ ID NO: 4).
- 1 10. The isolated nucleic acid molecule of claim 6 comprising nucleotide sequence of
2 HCVR 22 (SEQ ID NO: 5).
- 1 11. The isolated nucleic acid molecule of claim 6 comprising nucleotide sequence of
2 HCVR 24 (SEQ ID NO: 6).
- 1 12. A stable cell line transfected with the isolated nucleic acid molecule according to
2 claim 1, wherein said cell line:

- 1 20. A method of screening for anti-HCV therapeutics, which method comprises
2 comparing a level of HCV subgenomic replicon RNA or replicon RNA-associated
3 protein expression in the cell line of claim 12 contacted with a candidate therapeutic
4 agent to the cell line not contacted with the candidate therapeutic agent, wherein a
5 decrease in the level of HCV subgenomic replicon RNA or replicon RNA-associated
6 protein expression is indicative of the inhibitory activity of the agent.
- 1 21. A method for detecting antibodies to HCV in a biological sample from a subject
2 comprising contacting said sample with the protein fractions derived from the cell line
3 of claim 12 under conditions that permit interaction of HCV-specific antibodies in the
4 sample with the HCV protein(s) produced in said cell line, followed by detecting
5 binding of the antibodies in the sample to these HCV-derived protein(s), wherein said
6 binding is indicative of the presence of HCV infection in the subject from which the
7 sample was derived.
- 1 22. The method of claim 21 wherein said biological sample is selected from the group
2 consisting of blood, serum, plasma, blood cells, lymphocytes, and liver cells.